P. . ENT COOPERATION TREA: .

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 09 June 1998 (09.06.98)	
International application No. PCT/IB97/01627	**Applicant's or agent's file reference** 0785.039PC04
International filing date (day/month/year) 24 October 1997 (24.10.97)	**Priority date** (day/month/year) 25 October 1996 (25.10.96)
Applicant MOSE LARSEN, Peter et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

22 May 1998 (22.05.98)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Nicola Wolff
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

2072177

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)
0785.039PC04		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB97/01627	24/10/1997	25/10/1996
International Patent Classification (IPC) or national classification and IPC		
C12N15/12		
Applicant		
MOSE LARSEN, Peter et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22/05/1998	13.01.99
Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Roscoe, R Telephone No. (+49-89) 2399-2554

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB97/01627

I. Basis of the r port

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-84 as originally filed

Claims, No.:

1-27 as originally filed

Drawings, sheets:

1/47-47/47 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 12-13 ,(7-11 and 14-27 (partially)).

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 12-13 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 7-27 (partially).

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-6 and 7-27 (partially).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	(8-11, 14-27)(partially)
	No:	Claims	1-7
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11, 14-27
Industrial applicability (IA)	Yes:	Claims	1-18, 27
	No:	Claims	19-26(?)

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Citations

The documents mentioned in the present International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc. A transcript of the oral presentation D2 is not available.

---

1. **Unallowable amendments (Art.34(2)(b), PCT)**

The content of amended figure pages 40/47, 41/47 and 45/47 goes beyond the original disclosure of the filed application documents. Although applicant merely wishes to correct an error, the nature of correction necessary cannot be ascertained from the original documents (since these do not disclose the numbers obscured by overlap in the original versions). Hence, the amendments are unallowable.

2. **Unity (Section IV)**

The authorized authority entirely agrees with the non-unity objection raised in the International Search Report (Form PCT/ISA/210).

3. **Reasoned statement on Novelty, Inventive Step and Industrial Applicability (Section V)**

3.1 **Novelty (Art.33(2) PCT)**

D1 is the closest prior art. Said document discloses study of islet protein expression during onset of diabetes. The studies involved transplanting neonatal BB-DP rat islets in BB-DP rats. Rats were killed at a fixed time-point thereafter and part of the transplant was [35S]-methionine labelled for subsequent 2D-gel electrophoresis (2DGE). A number of undisclosed proteins were identified which were upregulated during onset of the disease.

Hence, D1 anticipates claims 1-7. The further claims are only being examined insofar as they relate to IEF010. The authorized authority has been unable to find such a protein in the prior art, possibly due to the lack of available sequence information. Hence, claims 8-11 and 14-27 are presently regarded as novel insofar as they relate to IEF010.

3.2 Inventive Step (Art.33(3) PCT)

Given that IEF010 was identified by the performance of a known method for isolating just this kind of protein (D1), said protein cannot be considered inventive. IEF010 is merely one of a large number of diabetes-mediating proteins. Its selection cannot at present be considered purposive, nor is any surprising property of the protein evident (indeed no functional properties of the protein are known).

Methods involving expressing IEF010 and looking for its effect on cells are obvious and routine given the circumstances of isolation of the protein (i.e it has been isolated due to its possible effect on islet cells). This is the case irrespective of whether in vitro methods or those involving transgenic animals are applied. Further, identification of modulators of the compound is an obvious procedure (assessment of modulators of diabetes-mediating proteins is disclosed in D3, for example).

3.3 Industrial Applicability (Art.33(4) PCT)

For the assessment of the present claims 19-26 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. Certain observations (Section VIII)

4.1 **Clarity (Art.6 PCT)**

Claim 6 is an inadmissible product-by-process style claim. The patentability of a product per se is not affected by the process of its production. The same applies to claim 18.

It is noted that no claim 12 is present and that claim 13 is thus also not assessible.

Claim 14 appears to be a method for distinguishing between protective or deleterious proteins, not as the wording implies a method of identifying either.

Claim 15 is worded unclearly due to the phrase "expressing a diabetes-mediating protein under conditions in which said protein is expressed".

Claim 17 - Statements that merely appear to anticipate the results of the method are unnecessary and confusing (i.e. "wherein said compounds are capable...", "wherein said compound inhibits..."). Indeed the purpose of the method and what is actually measured in step (b) is unclear. Furthermore, it would seem that claims 17 and 27 refer to similar, if not identical, matter. Such duplication of independent claims is unacceptable.

4.2 Lack of support in the description

Insofar as claims 8-11 and 14-27 relate to IEF010, the authorized authority consider these claims to lack support in the description. IEF010 has merely been characterized by M.W(125,500), pI (7.27) and by mass spectroscopy of a trypsin digest of the protein-comprising gel-spot (NB: not a purified protein). Thus, the IEF010 gene is not available to the skilled person. Neither is a method of purifying IEF010 in sufficient amounts for functional testing known. Hence, all claims relating to the use of the gene or purified protein lack support in the description (i.e. claims 11, 14-27).

Further, the medical potential of IEF010 is absolutely unknown and there is thus no basis for claims relating to its use for treating diabetes (administration could even make the condition worse) - claims 17-26

PATENT COOPERATION TREATY

US

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
0785.039PC04		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB 97/01627	24/10/1997	25/10/1996
Applicant		
MOSE LARSEN, Peter et al		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 28 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ **Certain claims were found unsearchable** (see Box I).

2. ☒ **Unity of invention is lacking** (see Box II).

3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - ☒ filed with the international application.
   - ☐ furnished by the applicant separately from the international application,
     - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - ☐ Transcribed by this Authority

4. With regard to the **title,**
   - ☒ the text is approved as submitted by the applicant.
   - ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   - ☒ the text is approved as submitted by the applicant.
   - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:
   Figure No. 2
   - ☐ as suggested by the applicant.
   - ☐ because the applicant failed to suggest a figure.
   - ☒ because this figure better characterizes the invention.
   - ☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 97/01627

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 19-26 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see annex

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6 and partially 7-27 (subject 1)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6 and partially 7-27

An in vivo method for identifying a diabetes-mediating protein comprising :

a) obtaining cells or tissue which secrete insulin or are capable of developing into insulin-secreting cells;
b) transplanting said cells or tissue into a host mammal, wherein said host mammal is at risk for development of diabetes;
c) removing said transplanted cells or tissue from said host mammals at a plurality of time periods between transplantation and development of diabetes:
d) analyzing the expression of said removed cells or tissue,
e) comparing the expression of said protein at one time period in the presence of diabetes development with the expression of said protein in the absence of diabetes development to identify a protein which exhibit an altered expression as a result of development of diabetes, wherein said protein is a diabetes-mediating protein;
the diabetes-mediating protein IEF 010 of table 1; methods using thereof for predicting the development of diabetes and identifying in vitro and in vivo the protective or deleterious effect of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

2. Claims: partially 7-27

the diabetes-mediating protein IEF 011 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

3. Claims: partially 7-27

the diabetes-mediating protein IEF 025 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

4. Claims: partially 7-27

the diabetes-mediating protein IEF 028 of table 1; in vitro and in vivo methods of identifying the protective or

deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

5. Claims: partially 7-27

the diabetes-mediating protein IEF 083 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

6. Claims: partially 7-27

the diabetes-mediating protein IEF 085 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

7. Claims: partially 7-27

the diabetes-mediating protein IEF 115 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

8. Claims: partially 7-27

the diabetes-mediating protein IEF 145 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

9. Claims: partially 7-27

the diabetes-mediating protein IEF 173 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a

transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

10. Claims: partially 7-27

the diabetes-mediating protein IEF 186 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

11. Claims: partially 7-27

the diabetes-mediating protein IEF 187 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

12. Claims: partially 7-27

the diabetes-mediating protein IEF 189 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

13. Claims: partially 7-27

the diabetes-mediating protein IEF 194 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

14. Claims: partially 7-27

the diabetes-mediating protein IEF 201 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous

diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

15. Claims: partially 7-27

the diabetes-mediating protein IEF 210 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

16. Claims: partially 7-27

the diabetes-mediating protein IEF 217 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

17. Claims: partially 7-27

the diabetes-mediating protein IEF 225 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

18. Claims: partially 7-27

the diabetes-mediating protein IEF 265 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

19. Claims: partially 7-27

the diabetes-mediating protein IEF 267 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

vivo using this animal or in vitro,for screening compounds and uses thereof.

20. Claims: partially 7-27

the diabetes-mediating protein IEF 276 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro,for screening compounds and uses thereof.

21. Claims: partially 7-27

the diabetes-mediating protein IEF 279 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods in vivo using this animal or in vitro,for screening compounds and uses thereof.

22. Claims: partially 7-27

the diabetes-mediating protein IEF 285 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods in vivo using this animal or in vitro,for screening compounds and uses thereof.

23. Claims: partially 7-27

the diabetes-mediating protein IEF 289 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

24. Claims: partially 7-27

the diabetes-mediating protein IEF 306 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds

and uses thereof.

25. Claims: partially 7-27

the diabetes-mediating protein IEF 310 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

26. Claims: partially 7-27

the diabetes-mediating protein IEF 329 GR78 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

27. Claims: partially 7-27

the diabetes-mediating protein IEF 329 NCPR of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

28. Claims: partially 7-27

the diabetes-mediating protein IEF 330 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

29. Claims: partially 7-27

the diabetes-mediating protein IEF 342 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

30. Claims: partially 7-27

the diabetes-mediating protein IEF 347 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

31. Claims: partially 7-27

the diabetes-mediating protein IEF 354 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

32. Claims: partially 7-27

the diabetes-mediating protein IEF 382 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

33. Claims: partially 7-27

the diabetes-mediating protein IEF 387 T064 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

34. Claims: partially 7-27

the diabetes-mediating protein IEF 387 TCPG of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

35. Claims: partially 7-27

the diabetes-mediating protein IEF 387 COPD of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

36. Claims: partially 7-27

the diabetes-mediating protein IEF 425 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

37. Claims: partially 7-27

the diabetes-mediating protein IEF 471 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

38. Claims: partially 7-27

the diabetes-mediating protein IEF 480 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

39. Claims: partially 7-27

the diabetes-mediating protein IEF 483 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

40. Claims: partially 7-27

the diabetes-mediating protein IEF 505 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

41. Claims: partially 7-27

the diabetes-mediating protein IEF 506 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

42. Claims: partially 7-27

the diabetes-mediating protein IEF 507 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

43. Claims: partially 7-27

the diabetes-mediating protein IEF 561 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

44. Claims: partially 7-27

the diabetes-mediating protein IEF 563 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

45. Claims: partially 7-27

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

the diabetes-mediating protein IEF 655 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

46. Claim : partially 727

the diabetes-mediating protein IEF 759 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

47. Claims: partially 7-27

the diabetes-mediating protein IEF 1081 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

48. Claims: partially 7-27

the diabetes-mediating protein IEF 1196 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

49. Claims: partially 7-27

the diabetes-mediating protein IEF 1342 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

50. Claims: partially 7-27

the diabetes-mediating protein IEF 1356 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

51. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 017 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

52. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 156 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

53. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 169 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

54. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 203 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

55. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 269 ANX2 of table 1;

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

56. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 269 G3P of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

57. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 298 LEG3 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

58. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 203 (unknown) of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

59. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 668 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

60. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 670 of table 1; in vitro and in vivo methods of identifying the protective or

deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

61. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 672 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

62. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 673 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

63. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 674 of table 1; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

64. Claims: partially 7-27

the diabetes-mediating protein IEF 015 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

65. Claims: partially 7-27

the diabetes-mediating protein IEF 339 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a

transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

66. Claims: partially 7-27

the diabetes-mediating protein IEF 340 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

67. Claims: partially 7-27

the diabetes-mediating protein IEF 344 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

68. Claims: partially 7-27

the diabetes-mediating protein IEF 358 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

69. Claims: partially 7-27

the diabetes-mediating protein IEF 436 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

70. Claims: partially 7-27

the diabetes-mediating protein IEF 441 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous

diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

71. Claims: partially 7-27

the diabetes-mediating protein IEF 442 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

72. Claims: partially 7-27

the diabetes-mediating protein IEF 484 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

73. Claims: partially 7-27

the diabetes-mediating protein IEF 510 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

74. Claims: partially 7-27

the diabetes-mediating protein IEF 614 ERP5 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

75. Claims: partially 7-27

the diabetes-mediating protein IEF 614 ATPB of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in

vivo using this animal or in vitro, for screening compounds and uses thereof.

76. Claims: partially 7-27

the diabetes-mediating protein IEF 665 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

77. Claims: partially 7-27

the diabetes-mediating protein IEF 719 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

78. Claims: partially 7-27

the diabetes-mediating protein IEF 825 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

79. Claims: partially 7-27

the diabetes-mediating protein IEF 831 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

80. Claims: partially 7-27

the diabetes-mediating protein IEF 882 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds

and uses thereof.

81. Claims: partially 7-27

the diabetes-mediating protein IEF 887 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

82. Claims: partially 7-27

the diabetes-mediating protein IEF 895 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

83. Claims: partially 7-27

the diabetes-mediating protein IEF 908 ER31 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

84. Claims: partially 7-27

the diabetes-mediating protein IEF 908 PMGB of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

85. Claims: partially 7-27

the diabetes-mediating protein IEF 939 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

86. Claims: partially 7-27

the diabetes-mediating protein IEF 941 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

87. Claims: partially 7-27

the diabetes-mediating protein IEF 949 RNU53882 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

88. Claims: partially 7-27

the diabetes-mediating protein IEF 949 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

89. Claims: partially 7-27

the diabetes-mediating protein IEF 950 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

90. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 001 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

91. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 007 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

92. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 009 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

93. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 018 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

94. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 102 TCPZ of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

95. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 102 RNPKMPS of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

96. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 123 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

97. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 129 KPY2 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

98. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 129 (unknown) of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

99. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 130 MMSA of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

100. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 130 RNPKMPS of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

101. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 171 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

102. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 174 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

103. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 176 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

104. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 181 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

105. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 182 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

106. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 211 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

107. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 227 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

108. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 231 BKCRU of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

109. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 231 BTHIL of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

110. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 236 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

111. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 253 of table 2; in

vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

112. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 296 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

113. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 306 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

114. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 310 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

115. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 326 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

116. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 328 of table 2; in vitro and in vivo methods of identifying the protective or

deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

117. Claims: partially 7-27

the diabetes-mediating protein NEPHGE 334 of table 2; in vitro and in vivo methods of identifying the protective or deleterious effects of this diabetes-mediating protein; a transgenic non-human mammal comprising the exogenous diabetes-mediating protein transgene and assay methods, in vivo using this animal or in vitro, for screening compounds and uses thereof.

INTERNATIONAL SEARCH REPORT

Interna[redacted] Application No
PCT/IB 97/01627

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/47 A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K A61K A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHRISTENSEN, U.B. ET AL.: "Protein expression at diabetes onset in BB-rats differs from that seen during islet allograft rejection" DIABETOLOGIA, vol. 38, no. suppl. 1, 1995, page A85 XP002062765 see abstract 327	1-7
O,X	& 31st annual meeting of the european association for the study of diabetes, STOCKHOLM, SWEDEN, September 12-16 1995 see the whole presentation --- -/--	1-7

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
21 April 1998	10. 08. 1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	CHAMBONNET, F

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ANDERSEN, H.U. ET AL.: "Two-dimensional gel electrophoresis of rat islet proteins. Interleukin 1Beta-induced changes in protein expression are reduced by L-arginine depletion and nicotinamide" DIABETES, vol. 44, no. 4, April 1995, pages 400-407, XP002062766 see the whole document	7-9
T	POCIOT, F. ET AL.: "A comprehensive approach to identifying new susceptibility genes to insulin-dependent diabetes mellitus: combining proteome and genome analysis" CYTOKINE, vol. 9, no. 11, November 1997, page 899 XP002062767 see abstract & Fifth annual conference of the international cytokine society, Lake Tahoe, USA. November 9-13 1997, see the whole document	1
T	KARLSEN, A.E. ET AL.: "Identification and characterization of proteins involved in cytokine mediated beta-cell destruction and insulin-dependent diabetes mellitus" CYTOKINE, vol. 9, no. 11, November 1997, page 912 XP002062768 see abstract	1